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### Deposited in DRO:

29 January 2016

### Version of attached file:

Accepted Version

### Peer-review status of attached file:

Peer-reviewed

### Citation for published item:

Heading, R.C. and Thomas, E.C.M. and Sandy, P. and Smith, G. and Fass, R. and Hungin, P.S. (2016) 'Discrepancies between upper GI symptoms described by those who have them and their identification by conventional medical terminology : a survey of sufferers in four countries.', *European journal of gastroenterology hepatology*, 28 (4). pp. 455-462.

### Further information on publisher's website:

<http://dx.doi.org/10.1097/MEG.0000000000000565>

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**Discrepancies between upper GI symptoms described by those who have them and their identification by conventional medical terminology: a survey of sufferers in four countries**

**Running head:** Upper GI symptoms as described by sufferers

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**Funding:** The study was commissioned and funded by Reckitt Benckiser. Writing support was provided by Cello Health and funded by Reckitt Benckiser.

**Conflict of Interests:** RCH has served as a paid advisor for Reckitt Benckiser and Takeda. APSH has received travel, advisory board and research funding from Reckitt Benckiser, Almirall and Shire. RF has served as a speaker for Takeda and Mederi Therapeutics, as an advisor for GlaxoSmithKline, Reckitt Benckiser and Vecta, and has received research support from Mederi Therapeutics and Ironwood Pharmaceuticals.

**Authors Contributions:** PS was the only author involved in development of the questionnaire, conduct of the survey and acquisition of the data. GS performed the statistical analyses. RCH and ECMT took lead roles in data interpretation and drafting the manuscript. RF and APSH were involved in the analysis and interpretation of the data and in drafting and critical revision of the manuscript.

## **ABSTRACT**

### **Objective**

We aimed to develop a self-administered questionnaire for upper GI symptoms based on lay vocabulary uninfluenced by established medical terminology or concepts and to conduct a survey of symptom occurrence among sufferers in four countries.

### **Methods**

The questionnaire was designed by integrating information gained from the vocabulary used by 38 upper GI symptom sufferers. There was no medical input to its development. The questionnaire was then used, after appropriate translation, in Brazil, Russia, the UK and the USA. Details of 10,659 symptom episodes were obtained from 2,665 individuals.

### **Results**

Nine symptoms described in lay vocabulary were identified during questionnaire development. Of these, one corresponded with regurgitation while two that were distinguished by survey participants might both be interpreted as heartburn. One chest symptom for which a corresponding medical term was uncertain occurred in some 30% of respondents. Five different 'stomach' or abdominal symptoms were identified. The predominant symptom and the pattern of concurrent symptoms often varied from one symptom episode to another. Use of the terms 'heartburn', 'reflux', 'indigestion' and 'burning stomach' to describe symptoms varied between countries.

### **Conclusion**

Some common upper GI symptoms described by those who suffer them have no clear counterpart in conventional medical terminology. Inadequacy of the conventional terminology

in this respect deserves attention: first, to characterize it fully, and thereafter to construct enquiry that delivers more precise symptom identification. Our results suggest that improvement may require use of the vocabulary of individuals suffering the symptoms without imposing conformity with established symptom concepts.

**Keywords:** Upper gastrointestinal tract, symptoms, questionnaires, gastroesophageal reflux, heartburn, dyspepsia, humans, vocabulary,

## **INTRODUCTION**

Most studies of upper GI symptom occurrence are founded on the use of questionnaires.

Various methodologies have been used to develop them but patient input into their development has become the norm (1-8). For example, the Glasgow Dyspepsia Questionnaire (1), the Global Overall Symptom scale (2), the Leeds Dyspepsia Questionnaire (3), the Nepean Dyspepsia Index (4), the RDQ (5), ReQuest (6), and the REFLUX questionnaire (7) have all utilised information obtained from patients in designing the questionnaires. Self-administered questionnaires have been favoured in recent years with involvement of focus groups to help formulate the wording of questions that will be readily understood by patients (4-7). This 'patient-friendly' wording is then reconciled with established medical terminology, which is the basis of subsequent analysis. To our knowledge no survey has yet used an upper GI symptom questionnaire constructed using layperson-based language without reference to the established medical symptom vocabulary.

Our study aimed to create a self-administered questionnaire for upper GI symptoms using lay vocabulary without imposition of medical terminology or concepts and to use it in a survey of symptom occurrence among sufferers in 4 countries.

## **METHODS**

### **Survey content**

The survey and online diary were developed, undertaken and the responses collated by two specialist market research companies (Winkle BV, Keizersgracht, Amsterdam, The Netherlands and Msi-aci BV, Joop Geesinkweg, Amsterdam, The Netherlands).

Starting from the range of symptoms given in the ROME III criteria for functional GI disorders, lay terminology was developed to describe possible upper GI symptoms. It was then tested and modified according to a series of qualitative one-to-one interviews carried out in Brazil,

Russia, the UK and the USA. Market research agency screening in these countries identified 38 subjects aged 18–64 years who had experienced upper GI symptoms within the previous 3 months; eight subjects in Brazil and 10 each in Russia, the UK and the USA. The outputs from these interviews were integrated to generate the questions used in the survey questionnaire.

The questionnaire and diary were first drafted in English and then translated by a professional translation agency into the local languages. The moderators who conducted the qualitative interviews reviewed the questionnaire to ensure the translations accorded with their findings.

### **Screening and extended survey**

Members of a market research panel were invited by email to complete the questionnaire entitled 'New Survey about Health Issues'. The invitees, aged 18–64 years, in Brazil, Russia, the UK and the USA were drawn at random from the market research panel. Panel membership required that the individual was responsible, either mainly or jointly, for shopping for medicines/medications.

This initial screening survey consisted of a demographic questionnaire and questions to establish whether the subject had experienced any of the specified upper GI symptoms in the appropriate part of the body within the last 3 months (Figure 1). Individuals answering positively were allowed access to an extended survey, which asked about the last symptom episode in more depth, including a question about what term they would use to describe their ailment to a doctor or to a friend.

Sufficient sample size was required at the diary stage to allow for the creation of a robust occasion-based segmentation. A target respondent sample size of 450 per country was set with this in mind. Allowing for a drop-out rate of 50% between the survey and diary stages, this led to a target sample size of approximately 900 per country at the initial survey.

### **Online diary**

Participants who entered the diary phase were emailed a link each day for up to 6 weeks between June and August 2010. They were asked to indicate whether they had experienced any of the listed symptoms that day in the labeled areas of their body (Appendix 1; symptom locations as shown in Figure 1). The participants were then asked more detailed questions concerning up to seven symptom episodes that occurred on different days during the 6-week period. The information requested included identification of the predominant (most intense) symptom on each occasion, rating its severity as mild, average or severe and indicating its duration, timing and location (Appendix 1). Answers to other questions about psychological and emotional responses to the symptoms, any actions taken and medications used in an attempt to gain relief are not reported in this paper and so the relevant questions are omitted from Appendix 1.

### **Statistical analysis of symptoms**

Data were analyzed using SAS software and descriptive statistics compiled according to the following populations: 1) survey responders; 2) survey and diary responders; 3) survey and diary responders with more than one diary episode; 4) all episodes in diary. Analysis was performed with all nine symptoms as reported by responders and, subsequently, by symptoms partly grouped according to medical terminology. For this latter purpose, positive responses to question 1 (Figure 1) were considered to be regurgitation, to question 3 to be heartburn and to questions 4, 5, 7, 8 or 9 to be dyspepsia. Owing to uncertainty about the appropriate medical term for symptoms represented by questions 2 and 6, no conventional medical term was applied to them and they are abbreviated hereafter to 'sharp rising pain: food pipe' and 'blocked feeling: chest', respectively.

The binomial outcomes collected at a participant level were compared between gender and age group (<45, ≥45) using a chi-square test.

The ordinal outcomes collected at a participant level were analyzed using a logistic regression model, with country as a fixed effect. Pairwise comparisons between countries were conducted from these models.

The binomial or ordinal outcomes collected per symptom episode across online diary participants were analyzed using logistic regression models with either gender, age group (<45, ≥45) or country included as a fixed effect and participant as a random effect. Pairwise comparisons between countries were conducted from these models.

## **RESULTS**

### **Survey and diary completion**

The screening survey identified a total of 5,158 subjects with the specified upper GI symptoms in the appropriate part of the body within the previous 3 months. Of these, 2,665 provided diary responses relating to 10,659 symptom episodes. Demographic data are shown in Table 1.

### **Incidence of symptoms as described in online diary**

Table 2 shows the symptoms reported by participants. 'Uncomfortably full / heavy stomach after a regular sized meal' and 'bitter or acidic taste in the back of the throat or mouth' (regurgitation) were the most frequent; 'burning sensation in the middle of the abdomen' was the least frequently reported. 'Blocked feeling or sensation that something is caught in the chest' and the bitter or acidic taste occurred with similar frequency in all countries. Some other symptoms such as the burning sensation in the chest and burning sensation in the stomach showed statistically significant differences between countries but the relative



frequency of the nine symptoms was broadly similar in all. Most symptoms were equally frequent in male and female participants but more frequent in the older than the younger age group.

**Table 1. Demographic data of the eligible respondents of the screening survey and diary completers.**

		SCREENING SURVEY	ONLINE DIARY
<b>Total number invited to take part</b>		93,686	–
<b>Total number who participated</b>		12,457	–
<b>Total number of eligible subjects</b>		5,158 (100%)	2,665 (100%)
<b>Gender</b>	<b>Male</b>	1,770 (34.4%)	864 (32.4%)
	<b>Female</b>	3,388 (65.7%)	1,801 (67.6%)
<b>Age group (years)</b>	<b>18–24</b>	494 (9.6%)	242 (9.1%)
	<b>25–34</b>	1,264 (24.5%)	698 (26.2%)
	<b>35–44</b>	1,105 (21.4%)	591 (22.2%)
	<b>45–54</b>	1,149 (22.3%)	611 (22.9%)
	<b>55–64</b>	1,146 (22.2%)	523 (19.6%)
	<b>&lt;45</b>	2,863 (55.5%)	1,531 (57.4%)
	<b>≥45</b>	2,295 (44.5%)	1,134 (42.6%)
<b>Country</b>	<b>Brazil</b>	944 (18.3%)	583 (21.9%)
	<b>Russia</b>	1,431 (27.7%)	814 (30.5%)
	<b>United Kingdom (UK)</b>	1,429 (27.7%)	691 (25.9%)
	<b>United States (US)</b>	1,354 (26.3%)	577 (21.7%)

**Table 2. Incidence of online diary reported symptoms.**

	Bitter/ acidic taste N (%)	Sharp rising pain: food pipe N (%)	Burning sensation: chest N (%)	Burning sensation: abdomen N (%)	Burning sensation: stomach N (%)	Blocked feeling: chest N (%)	Dull ache: abdomen N (%)	Dull ache: stomach N (%)	Heavy stomach
All	1490 (55.9)	752 (28.2)	892 (33.5)	728 (27.3)	816 (30.6)	783 (29.4)	994 (37.3)	1245 (46.7)	1613 (60.5)
Brazil	312 (53.5)	150 (25.7) <sup>c</sup>	192 (32.9) <sup>f</sup>	214 (36.7) <sup>i</sup>	303 (52.0) <sup>l</sup>	158 (27.1)	200 (34.3)	256 (43.9)	364 (62.4)
Russia	452 (55.5)	172 (21.1)	180 (22.1)	163 (20.0)	186 (22.9)	234 (28.7)	279 (34.3)	371 (45.6)	509 (62.5)
UK	387 (56.0)	245 (35.5) <sup>b</sup>	275 (39.8) <sup>e</sup>	159 (23.0) <sup>h</sup>	137 (19.8) <sup>k</sup>	223 (32.3) <sup>m</sup>	268 (38.8)	350 (50.7) <sup>o</sup>	414 (59.9)
US	339 (58.8)	185 (32.1) <sup>a</sup>	245 (42.5) <sup>d</sup>	192 (33.3) <sup>g</sup>	190 (32.9) <sup>j</sup>	168 (29.1)	247 (42.8) <sup>n</sup>	268 (46.4)	326 (56.5) <sup>p</sup>
Male	481 (55.7)	237 (27.4)	291 (33.7)	245 (28.4)	284 (32.9)	253 (29.3)	283 (32.8)	365 (42.2)	521 (60.3)
Female	1009 (56.0)	515 (28.6)	601 (33.4)	483 (26.8)	532 (29.5)	530 (29.4)	711 (39.5) <sup>q</sup>	880 (48.9) <sup>r</sup>	1092 (60.6)
<45	813 (53.1)	374 (24.4)	440 (28.7)	370 (24.2)	448 (29.3)	408 (26.6)	517 (33.8)	711 (46.4)	938 (61.3)
≥45	677 (59.7)	378 (33.3) <sup>t</sup>	452 (39.9) <sup>t</sup>	358 (31.6) <sup>t</sup>	368 (32.5)	375 (33.1) <sup>u</sup>	477 (42.1) <sup>t</sup>	534 (47.1)	675 (59.5)

N=number of respondents and (%) refers to the percentage who answered “yes” for each question.

*Statistics for countries:*

<sup>a</sup>*p*=0.0175 vs. Brazil, *p*<0.0001 vs. Russia; <sup>b</sup>*p*<0.0002 vs. Brazil, *p*<0.0001 vs. Russia; <sup>c</sup>*p*=0.0447 vs. Russia; <sup>d</sup>*p*<0.0008 vs. Brazil, *p*<0.0001 vs. Russia; <sup>e</sup>*p*=0.0114 vs. Brazil, *p*<0.0001 vs. Russia; <sup>f</sup>*p*<0.0001 vs. Russia; <sup>g</sup>*p*<0.0001 vs. UK and Russia; <sup>h</sup>*p*<0.0001 vs. Brazil; <sup>i</sup>*p*<0.0001 vs. Russia; <sup>j</sup>*p*<0.0001 vs. UK, Brazil and Russia; <sup>k</sup>*p*<0.0001 vs. Brazil; <sup>l</sup>*p*<0.0001 vs. Russia; <sup>m</sup>*p*=0.0448 vs. Brazil; <sup>n</sup>*p*=0.0030 vs. Brazil, *p*=0.0012 vs. Russia; <sup>o</sup>*p*=0.0165 vs. Brazil, *p*=0.0497 vs. Russia; <sup>p</sup>*p*=0.0396 vs. Brazil, *p*=0.0238 vs. Russia.

*Statistics for gender:*

<sup>q</sup>*p*=0.0008; <sup>r</sup>*p*=0.0014

*Statistics for age:*

<sup>s</sup>*p*=0.0007; <sup>t</sup>*p*<0.0001; <sup>u</sup>*p*=0.0003

## Predominant symptoms

### Symptom predominance and severity

When the five symptoms comprising ‘dyspepsia’ were considered as one entity, it was the most commonly reported predominant symptom, being identified as such by 2,121 (79.6%) of participants during at least one episode. ‘Bitter/acidic taste’ (regurgitation) was reported as the predominant symptom at least once by 1,158 (43.5%) participants, ‘burning sensation: chest’ (heartburn) by 525 (19.7%), ‘blocked feeling: chest’ by 443 (16.6%) and ‘sharp rising pain: food pipe’ by 385 (14.4%) participants.

The frequency with which each of the five symptoms was reported as predominant varied by country ( $p \leq 0.0022$ , see Figure S1 in the online supplementary material). Notable differences were observed for 'blocked feeling: chest', which was most frequent in Russia (164; 20.1%) and least frequent in Brazil (60; 10.3%), and 'burning sensation: chest' had a higher prevalence in the UK (187; 27.1%) and the USA (146; 25.3%) compared with Brazil (78; 13.4%) and Russia (114; 14.0%). Reports of 'sharp rising pain: food pipe' as the predominant symptom were highest among subjects in the UK (147; 21.3%) and lowest among subjects in Brazil (52; 8.9%).

Reported severity of the symptoms varied by country (Figure 2). Overall, the predominant symptoms were mostly classed as 'average' in severity (51.2%); 38% were classed 'mild' and 10.9% 'severe'. Subjects in Brazil less often reported their predominant symptom as severe (3.5%) compared with the USA (11.3%), UK (13.0%) and Russia (12.8%), and also rated their predominant symptom as mild (57%) more often than subjects in the USA (38.7%), UK (35.3%) and Russia (28.4%) ( $p < 0.0001$  for all comparisons).

The predominant symptom varied in 67% of those who reported more than one symptom episode. Two different predominant symptoms were reported on different occasions by 894 subjects (44%), three different symptoms by 359 (18%), four different symptoms by 101 (5%) and five different predominant symptoms by 13 (0.6%) (Figure 3).

#### *Predominant symptom timing*

Participants also recorded the time of day when their predominant symptom was at its strongest (Figure 4A). Overall, 'bitter/acidic taste' was most commonly reported in the morning upon waking (32.4%), whereas postprandial periods were particularly associated with the occurrence of other symptoms. 'Burning sensation: chest' was most commonly reported in the afternoon after lunch (20.1%) and at other times in the afternoon (20.5%). 'Sharp rising pain: food pipe' was most commonly reported after lunch (18.5%) and dinner (19.0%), with a

combined after lunch/dinner prevalence of 37.6%. 'Dyspepsia' was most common after lunch (23.8%) and dinner (23.2%), with a combined after lunch/dinner prevalence of 47.0%.

An effect of country on the prevalence of 'bitter/acidic taste' in the morning was observed ( $p < 0.0001$ ), with Brazil and Russia reporting an approximate twofold greater prevalence in this symptom at this time point (41.8% and 44.7%, respectively) than the USA and UK (21.5% and 21.0%, respectively). Pairwise comparisons for the USA or UK versus Brazil or Russia were all highly significant ( $p < 0.0001$ ). The prevalence of 'sharp rising pain: food pipe' after lunch/dinner also varied by country, with Russia having a significantly lower prevalence (23.7%) compared with the USA (37.0%;  $p = 0.0296$ ) and the UK (45.1%;  $p = 0.0008$ ), although not significantly versus Brazil (37.3%;  $p = 0.0554$ ).

#### *Predominant symptom duration*

The reported duration of predominant symptoms is shown in Figure 4B. 'Bitter or acidic taste in the back of the throat or mouth', 'sharp rising pain in the food pipe' and 'burning sensation or burning pain in the chest' were most commonly reported to last between 15 minutes and 1 hour (28.6%, 26.6% and 26.0%, respectively). 'Blocked feeling or sensation that something is caught in the chest' and 'dyspepsia' symptoms were most commonly reported to last between 1–2 hours (25.3% and 28.7%, respectively).

Overall, there were differences in duration of predominant symptoms between all countries except the USA and the UK ( $p < 0.0001$ ). Gender also demonstrated differences ( $p < 0.0001$ ).

There were no differences between age groups (see Supplementary Figures S2–S4).

#### **Symptom concurrence**

Across all episodes, multiple symptoms were reported on 28% of 10,603 occasions (Figure 5).

The discrepancy with the 10,659 symptom occasions shown in Figure 2 arose from failure to

complete Section A of the diary (Appendix 1) on 56 occasions. Dyspepsia accounted for most instances where a single symptom was reported (45% of all episodes), with 'bitter or acidic taste in the throat or mouth', 'blocked feeling or sensation that something is caught in the chest', 'burning sensation or burning pain in the chest' and 'sharp rising pain in the food pipe' being the single symptom in 15.6%, 3.9%, 5.3% and 2.5% of episodes, respectively. Overall, two concurrent symptoms were reported on 17.2% of occasions and the rates for simultaneously suffering three, four or five concurrent symptoms were 5.6%, 2.0% and 2.9%, respectively (Figure 5).

Particular attention was paid to the sharp rising pain in the food pipe and burning sensation or pain in the chest' in relation to the question of whether one or both should be considered to correspond to heartburn. There were 1,975 occasions on which respondents reported experiencing either the sharp rising pain in the food pipe or the burning sensation or pain in the chest and a further 659 occasions (in 348 individuals) on which the two were reported concurrently (Figure 5). In addition to the occasions when the two symptoms occurred concurrently, 58% of these individuals reported other occasions on which they experienced either the sharp rising pain in the food pipe' or the burning sensation or pain in the chest without the other.

#### **Correlation of patient language with symptom experience**

The screening survey asked participants what term they would use to describe their ailment. A high proportion (544; 56.8%) of people from Russia, who experienced 'bitter or acidic taste in the back of the throat or mouth', called it 'heartburn', with only 145 (15.2%) describing their symptom as reflux/acid reflux. In Brazil, 'heartburn' was also the most common patient descriptor for the bitter/acidic taste (238; 38.0%) compared with 187 (29.9%) who defined it as reflux/acid reflux. Interestingly, 92 (14.7%) participants in Brazil described 'bitter/acidic taste' as 'burning stomach', compared with 1.9% of respondents across the other countries. By contrast, reflux/acid reflux was the most common descriptor for the bitter/acidic taste in the back of the throat or mouth in the USA and the UK (448; 52.6% and 431; 48.4%, respectively).

The majority of subjects in the UK and the USA named their burning sensation in the chest as heartburn (397; 52.4% and 474; 51.9%, respectively). However, only 95 (22.1%) and 176 (29.1%) subjects in Brazil and Russia called this symptom heartburn; more commonly describing it as 'burning stomach' (89; 20.7%) in Brazil, 'indigestion' (98; 16.2%) in Russia or 'other' (111; 25.9% Brazil and 105; 17.4% Russia). 'Indigestion' was also used for 'burning sensation in the chest' by 263 (28.8%) UK subjects.

## DISCUSSION

Uncertainty about translating a patient's description of symptoms into established medical terminology is familiar to many physicians, who acknowledge that conventional terminology may not capture some aspects of symptom perception that patients describe. Nevertheless, we are not aware of any previous attempt at systematic creation of an upper GI symptom questionnaire from sufferers' own vocabulary without reference to conventional medical concepts or terminology. Our results describe the occurrence and patterns of these upper GI symptoms in 10,659 symptom episodes experienced by the questionnaire respondents.

Matching the lay vocabulary of our questionnaire with conventional medical symptom terminology revealed substantial disconnect between them. While the 'bitter or acidic taste in the back of the throat or mouth' may be interpreted as 'regurgitation', not least because it was prominent on waking in the morning (9), equating 'burning sensation or burning pain in the chest' with heartburn implies that heartburn was occurring only about two thirds as often as regurgitation in this population. Burning chest pain or discomfort is widely taken to be a description of heartburn in everyday clinical practice, though Carlsson et al. (10) advocated a definition in which the moving quality of the feeling was recognised ('a burning feeling rising from the stomach or lower chest up towards the neck') and asserted that this served to identify heartburn responsive to acid suppressing medication. However, if the 'burning sensation or burning pain in the chest' and the 'sharp rising pain in the food pipe' reported by our questionnaire respondents are considered just to be alternative descriptions of heartburn, combining the two implies that heartburn occurred more frequently than regurgitation. Nevertheless, the question of whether the 'burning sensation' and the 'sharp rising pain' are just alternative ways in which sufferers choose to describe the same sensation or are in fact two different sensations is obviously important if the symptoms are to be precisely identified. The fact that 58% of individuals who reported having the two symptoms concurrently on some occasions also reported having one without the other on other occasions implies they are not simply alternative descriptions of the same sensation. Consequently, use of the term 'heartburn' to denote both does not accurately represent the symptoms the sufferers themselves recognised.

The symptom 'blocked feeling or sensation that something is caught in the chest' is also problematic. At first, it might be thought to correspond with dysphagia but sufferers commonly reported the symptom duration as 1–2 hours, which seemingly points against a direct relationship with swallowing. No specific enquiry about swallowing or symptom relationships to swallowing was incorporated in the questionnaire and because the

questionnaire wording was designed without medical input, and subjects responded to the questions on-line, medically informed interrogation to characterise the nature of the symptom further was not possible within this study. Nevertheless, the question concerning the 'blocked feeling or sensation that something is caught in the chest' elicited positive responses in almost one third of respondents in all four countries and, of course, the question wording derived from the original interviews with those experiencing the symptom. It is therefore hard to refute a contention that this wording describes a sensation recognised and experienced by a significant proportion of individuals with upper GI symptoms. We can propose no immediately obvious counterpart in conventional medical terminology.

Unsurprisingly, dyspepsia was the most common symptom reported in all countries when the five symptoms perceived in the 'stomach' or abdomen were grouped together. Indeed, one or more of the symptoms comprising dyspepsia was reported by nearly all respondents in all four countries. The results add to existing evidence of overlap between reflux and dyspepsia symptoms (11-13), with 28% of respondents experiencing at least two symptoms concurrently on any one occasion. This figure corresponds closely with the findings of a community survey in which co-existing dyspepsia and reflux symptoms occurred in 24% of those reporting symptoms (12). This symptom overlap is a key issue in debate surrounding the definition of reflux disease and dyspepsia as separate or single entities (14), which is of course highly relevant to the challenge of accurate clinical diagnosis.

It is obvious that use of the single term 'dyspepsia' does not respect the fact that our study participants were describing five 'stomach' and abdominal symptoms they considered could be distinguished. Such conflation of symptoms itself raises potential problems for precision of diagnosis and for choice of treatment. Acknowledging this, the Rome III classification of functional dyspepsia refined earlier definitions by introducing a distinction between postprandial distress and epigastric pain syndromes. A form of enquiry to identify the former



has been proposed (15) but these two variants of functional dyspepsia often occur concurrently prompting some to suggest this classification is inherently unsatisfactory (16). However, better identification of symptoms gained from more detailed enquiry may be helpful (17,18). In addition, 'heartburn' is said to occur commonly in individuals with functional dyspepsia (14). Our results have shown that besides using the word 'dyspepsia' to describe five different symptoms, the single word 'heartburn' cannot properly represent both 'sharp rising pain in the food pipe' and 'burning sensation or pain in the chest'. Neither dyspepsia nor heartburn is a precise term, therefore. Greater precision is required for both if diagnosis and classification of upper GI disorders are to be improved.

Another aspect of our results with potential relevance to clinical practice is the observation that two-thirds of subjects reported different predominant symptoms on different occasions. To our knowledge, the magnitude of this variability has not been demonstrated previously. Some years ago it was reported that a diagnosis of reflux disease was likely to be correct if heartburn or regurgitation were clearly predominant symptoms (19). Subsequent consensus statements pointed out that while predominant heartburn was thought to permit a diagnosis of GORD in 75-80% of patients, this belief was based on clinical opinion rather than further evidence (20, 21). More recently, guidelines have simply advised that 'typical symptoms of heartburn and regurgitation' justify a presumptive GORD diagnosis (22). Our findings show that in many subjects both the predominant symptom and the pattern of concurrent symptoms vary from one symptom episode to the next. Only in one third of individuals is one symptom consistently predominant.

Apart from 'bitter or acidic taste in the back of the throat or mouth', which was most common on waking up in the morning, the majority of predominant symptoms occurred mainly after meals. The blocked feeling in the chest was most often reported after lunch, 'burning

sensation or burning pain in the chest' after lunch and in the afternoon whereas 'sharp rising pain in the food pipe' and the group of symptoms comprising dyspepsia were most commonly experienced after lunch and dinner.

The pattern of predominant nocturnal symptoms differed from daytime symptoms. The prevalence of nocturnal symptoms in our subjects was low compared with some reports (23) though not all investigators find nocturnal symptoms to be common (24). Our results were almost certainly influenced by inclusion of individuals with relatively mild symptoms and it is also possible our questionnaire did not reliably identify symptoms occurring during the 'recumbent awake' period, said to be especially important in reflux disease (25).

National differences in the medical term study subjects thought appropriate for their symptoms were evident in our results. Most obviously, the symptom identified in all 4 countries as 'bitter or acidic taste in the back of the throat or mouth' was termed heartburn by many Russian subjects and by some Brazilian subjects, whereas in the USA and UK it was mostly termed reflux. A burning sensation in the chest was considered by many subjects in the UK and USA to be heartburn, but less certainly identified as such in Brazil and Russia. National differences in vocabulary and symptom interpretation seem unlikely to be restricted to the lay population: it seems inevitable they will, to some degree, extend to physicians also. Thus, while translation of basic medical terms such as heartburn, reflux and regurgitation into different languages may be straightforward, the words may nevertheless have different nuanced meanings in different countries. Such differences have received little attention in formal studies but it is apparent that linguistic and cultural factors will influence a patient's understanding of their symptoms.

As our study respondents were members of market research panels, most of the findings can neither be directly compared with studies of unselected populations nor with studies of patients consulting physicians. Moreover, the low threshold of symptom frequency needed to

enter our study may also mean that the findings will differ from those reported in many publications. However, difficulty in matching some patients' descriptions of their symptoms with the conventional medical vocabulary is recognised by most clinicians. When developing questionnaires for self-administration, this potential difficulty has usually been addressed by devising symptom enquiry in a way that aims to optimise identification of the medically recognised symptoms (4-7, 26, 27). Typically, patients are provided with symptom descriptions, sometimes supported by word pictures, that expert opinion considers may be equated with the established medical vocabulary. It is assumed the established medical vocabulary can properly represent the patients' symptoms.

Our survey questionnaire was not designed to measure symptom burden and no suggestion is made that it would be suitable for this purpose. Rather, the study has demonstrated that the established medical terminology does not identify some commonly occurring upper GI symptoms that sufferers recognise when described using vocabulary generated by fellow sufferers. Symptom descriptions based on the vocabulary of individuals who suffer them merit closer attention with a view to characterising upper GI symptoms more precisely.

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## Legends

### Figure 1. Eligibility criteria.

Subjects were asked if they had experienced any of the following in the past 3 months. If so, they were asked “Where in your body did you feel this symptom was located?” and to respond with reference to the diagram.

\*See text for explanation of proposed medical terminology.

### Figure 2. Severity of predominant symptom by country.

P values relate to variability of predominant symptoms across episodes reported by individual subjects (ordinal logistic regression with random participant effect).

### Figure 3. Predominant symptoms reported by respondents across all their symptom episodes.

**Figure 4. Percentage of study participants who experienced the specified symptoms at their strongest at the stated time (A), and percentage of study participants who experienced the specified predominant symptoms for the stated durations (B).**

### Figure 5. Frequency of symptoms reported concurrently across 10,603 symptom episodes.

## Supplementary Information

### Appendix 1.

#### Figure S1. Frequency of symptoms identified by respondents as predominant

Pairwise comparisons: <sup>a</sup>p=0.006 vs. Russia, <sup>b</sup>p=0.040 vs. UK; p=0.0004 vs. Russia; <sup>c</sup>p=0.031 vs. Russia; <sup>d</sup>p=0.008 vs. US, p<0.0001 vs. UK and Russia; <sup>e</sup>p<0.0001 vs. US and UK; <sup>f</sup>p<0.0001 vs. US and UK; <sup>g</sup>p=0.020 vs. UK; <sup>h</sup>p=0.0003 vs. US and p<0.0001 vs. UK; <sup>i</sup>p=0.012 vs. US and p<0.0001 vs. UK; <sup>j</sup>p=0.0028 vs. Brazil and p=0.0062 vs. Russia; <sup>k</sup>p=0.0078 vs. Brazil and p=0.018 vs. Russia.

#### Figure S2. Duration of predominant symptom by country.

#### Figure S3. Duration of predominant symptom by age.

#### Figure S4. Duration of predominant symptom by gender.

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\*See text for explanation of proposed medical terminology.

### Table 1. Demographic data of the eligible respondents of the screening survey and diary completers.

### Table 2. Incidence of online diary reported symptoms.

N=number of respondents and (%) refers to the percentage who answered “yes” for each question.

*Statistics for countries:*

<sup>a</sup> $p=0.0175$  vs. Brazil,  $p<0.0001$  vs. Russia; <sup>b</sup> $p<0.0002$  vs. Brazil,  $p<0.0001$  vs. Russia; <sup>c</sup> $p=0.0447$  vs. Russia; <sup>d</sup> $p<0.0008$  vs. Brazil,  $p<0.0001$  vs. Russia; <sup>e</sup> $p=0.0114$  vs. Brazil,  $p<0.0001$  vs. Russia; <sup>f</sup> $p<0.0001$  vs. Russia; <sup>g</sup> $p<0.0001$  vs. UK and Russia; <sup>h</sup> $p<0.0001$  vs. Brazil; <sup>i</sup> $p<0.0001$  vs. Russia; <sup>j</sup> $p<0.0001$  vs. UK, Brazil and Russia; <sup>k</sup> $p<0.0001$  vs. Brazil; <sup>l</sup> $p<0.0001$  vs. Russia; <sup>m</sup> $p=0.0448$  vs. Brazil; <sup>n</sup> $p=0.0030$  vs. Brazil,  $p=0.0012$  vs. Russia; <sup>o</sup> $p=0.0165$  vs. Brazil,  $p=0.0497$  vs. Russia; <sup>p</sup> $p=0.0396$  vs. Brazil,  $p=0.0238$  vs. Russia.

*Statistics for gender:*

<sup>q</sup> $p=0.0008$ ; <sup>r</sup> $p=0.0014$

*Statistics for age:*

<sup>s</sup> $p=0.0007$ ; <sup>t</sup> $p<0.0001$ ; <sup>u</sup> $p=0.0003$

**Figure 4. Percentage of study participants who experienced the specified symptoms at their strongest at the stated time (A), and percentage of study participants who experienced the specified predominant symptoms for the stated durations (B).**

**Figure 5. Frequency of symptoms reported concurrently across 10,603 symptom episodes.**

### Supplementary Information

#### Appendix 1.

#### Figure S1. Frequency of symptoms identified by respondents as predominant

Pairwise comparisons: <sup>a</sup> $p=0.006$  vs. Russia, <sup>b</sup> $p=0.040$  vs. UK;  $p=0.0004$  vs. Russia; <sup>c</sup> $p=0.031$  vs. Russia; <sup>d</sup> $p=0.008$  vs. US,  $p<0.0001$  vs. UK and Russia; <sup>e</sup> $p<0.0001$  vs. US and UK; <sup>f</sup> $p<0.0001$  vs. US and UK; <sup>g</sup> $p=0.020$  vs. UK; <sup>h</sup> $p=0.0003$  vs. US and  $p<0.0001$  vs. UK; <sup>i</sup> $p=0.012$  vs. US and  $p<0.0001$  vs. UK; <sup>j</sup> $p=0.0028$  vs. Brazil and  $p=0.0062$  vs. Russia; <sup>k</sup> $p=0.0078$  vs. Brazil and  $p=0.018$  vs. Russia.

**Figure S2. Duration of predominant symptom by country.**

**Figure S3. Duration of predominant symptom by age.**

**Figure S4. Duration of predominant symptom by gender.**

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